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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,378	11/15/2001	Christopher P. Adams	018422-00031	4706

20350 7590 07/29/2003

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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/857,378	Adams et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 9, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above, claim(s) *58-65* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-57* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group I, claims 1-57 in Paper No. 9, filed 5/9/03, is acknowledged. The traversal is on the ground(s) that the product of Boles is not incorporated into a polymer, but into a complex.. This is not found persuasive because claim 1 does not specify the polymer. The first nucleic acid itself meets the limitation of the "polymer". Any nucleotide within nucleic acid contains ethylene moieties, e.g. any adjacent pairs of carbons in the ribose or deoxyribose and the 4 and 5 carbons of either the purine or pyrimidine bases. Also, the claim embraces any nucleic acid to which an ethylene moiety is attached to at least one nucleoside. Thus, the nucleic acid containing subunits of Boles, which are then co-polymerized with other ethylene-containing subunits, themselves meet the limitation of instant claim 1. Claim 1 of Boles is directed to such a "first subunit"; the "first polymerizable ethylene-containing monomer unit" is itself a polymer by virtue of both the nucleic acid and the poly (ethylene glycol) moieties. It comprises a nucleic acid derivatized to an α-acrylol, ω-N-hydroxysuccinimidyl ester of poly (ethylene glycol)-propionic acid. The "first subunit" of instant claim 1 could be the ethylene glycol subunit to which the nucleic acid is attached, or the nucleoside of the nucleic acid to which the ester is attached. In either case, the hydroxysuccinimidyl is a linker.

The requirement is still deemed proper and is therefore made FINAL.

Claims 58-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Information Disclosure Statement

The information disclosure statement filed 5/9/03 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but EP 0524864 referred to therein has not been considered. Also, only the English abstract of WO 98/17317 has been considered, since the remainder is in German, and no translation has been provided.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). The cover sheet of the published PCT application does not meet this requirement. An abstract on a separate sheet is required.

Claim Objections

Applicant is advised that should claim 1 be found allowable, claim 2 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). For the first subunit to be part of a polymer, it must be covalently attached to a second subunit.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, or in the alternative under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention..

The claims are directed to a polymer comprising a subunit which comprises nucleic acid, which is itself a polymer. The subunit is incorporated into the polymer "by using" a subunit precursor that comprises a nucleic acid and an ethylene-containing moiety. An ethylene group is basically two carbon atoms covalently bound to each other either by single or double bonds, and each carbon is covalently bound to at least one atom which is not hydrogen. Nucleotides themselves include several ethylene groups in the sugars, e.g ribose, and in the purine or pyrimidine bases. Consequently, some claims are broad enough to encompass nucleic acid itself, and nucleic acids complexed with histones (compacting moiety).

The claims do not specify the nature of the "polymer." The only polymer recited in all claims is nucleic acid. The first subunit precursor must comprise both a nucleic acid and an ethylene-containing moiety, but the relationship of either to the polymer is not defined. In addition, no claims except for claims 26 and 49 place any limits on subunits of the polymer beyond the first. Thus, the backbone of the "polymer" could be a polymer made by polymerization of ethylene groups, e.g. polyacrylamide or polyethylene glycol, where every subunit of the polymer contains an ethylene moiety. Alternatively, the polymer backbone could be a nucleic acid, or it could be a polymer made by polymerization of an unspecified moiety of the first subunit precursor other than an ethylene-containing moiety with other similar unspecified moieties of equally unspecified other subunits, e.g. amino acid-containing subunits with the polymer backbone being a polypeptide. Only the first of these three possibilities is described in the specification, i.e. where the ethylene group itself is the polymerizable group in

forming the backbone of the polymer with other subunits comprising polymerizable ethylene groups.

Since the claims potentially read on polymers very different in structure from the polymers described in the specification, the specification does not provide an adequate written description of the full scope of the claimed subject matter. Also, the disparity between the very general language of the claims with respect to the polymer and the much narrower scope of polymers described in the specification raises doubt as to what polymers are or are not embraced by the claims, i.e. the claims are vague with respect to the polymer backbone.

This rejection would be overcome by amending the claims to more adequately define the subunits in the backbone of the polymer, i.e. to clearly define the relationship of ethylene moieties in the polymer.

Claims 4, 9-12, 30-55 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "said second subunit" in line 2. Claims 9 and 32 recite the limitation "said linker arm" in line 1 of each. Claims 10 and 33 recite the limitation "said cleavable moiety" in line 1 of each. Claim 30 recites the limitation "said polymer" in line 2. Claim 57 recites the limitation "said polymer" in line 3. There is insufficient antecedent basis for these limitations in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-16, 19, 27, 30-39, 42, 53, 56, and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Tullis, US 4,904,582.

Tullis discloses water-soluble polymers (and particles) comprising a polymer made up of subunits with ethylene containing moieties, e.g. PEG, wherein single-strand oligonucleotides (nucleic acids) are covalently attached to individual ethylene containing subunits. The nucleic acids may be attached to polymer subunits via a linking group. The polymer itself enhances cellular uptake of the oligonucleotide. Polymer compositions are to be used *in vivo*, consequently the compositions are pharmaceutical compositions. See entire reference, especially col. 2, lines 45-58; col. 4, line 62 to col. 5, line 32; col. 6, lines 49-64; Examples 1-9; claims 8, 10, and 13-19.

Claims 1 and 30 recite an implied process of making the polymer wherein the nucleic acid is attached to an ethylene containing moiety, which is then polymerized with other ethylene-containing subunits. While the prior art does not teach making the polymer by this method, the prior art polymer could be made this way, so the recited method of making does not distinguish the prior art and claimed products. In so much as all chemical bonds can be cleaved by at least one of the processes recited in claim 5, for example, the limitations regarding "cleavable moiety" are met by any bond in the polymer, including bonds between subunits or between subunit and nucleic acid. Also, the nucleotide proximal to the polymer may be considered to be part of the "linker group" and the phosphodiester bond separating this nucleotide from the rest of the oligonucleotide is a cleavable bond of the linker group, and cleavable by a process in a biological system. With respect to "particle", e.g. claim 30, a particle is simply a "very small piece", consider "sub-atomic particle". Thus, a single polymer molecule meets this limitation, i.e. claim 30 embraces the subject matter of claims 1-29.

Claims 1-12, 17, 20-25, 27, 28, 30-35, 40, 43-48, 50, 51, 53, 56, and 57 are rejected under 35 U.S.C. 102(e) as being anticipated by Cook, US 6,172,208.

Cook discloses water-soluble polymers (and particles) comprising a methylacrylamide polymer backbone with oligonucleotides covalently attached to some subunits, hence a copolymer (see diagram at top of col. 9). The oligonucleotides are attached to the polymer subunits via a linker group. Polymer compositions are to be used *in vivo*, consequently the

compositions are pharmaceutical compositions, or *in vitro*. The oligonucleotide may, during use, hybridize with single strand nucleic acid of form triplexes with double strand nucleic acids. Where the nucleic acid is double-strand or triplex, one strand meets the limitation of compacting moiety relative to the another strand since it causes a random coiled single strand into a helical conformation. See entire reference, especially col. 7-9, 11-13, col. 14, lines 1-3; col. 16, lines 25-39.

Claims 1 and 30 recite an implied process of making the polymer wherein the nucleic acid is attached to an ethylene containing moiety, which is then polymerized with other ethylene-containing subunits. While the prior art does not teach making the polymer by this method, the prior art polymer could be made this way, so the recited method of making does not distinguish the prior art and claimed products. In so much as all chemical bonds can be cleaved by at least one of the processes recited in claim 5, for example, the limitations regarding "cleavable moiety" are met by any bond in the polymer, including bonds between subunits or between subunit and nucleic acid. Also, the nucleotide proximal to the polymer may be considered to be part of the "linker group" and the phosphodiester bond separating this nucleotide from the rest of the oligonucleotide is a cleavable bond of the linker group, and cleavable by a process in a biological system. With respect to "particle", e.g. claim 30, a particle is simply a "very small piece", consider "sub-atomic particle". Thus, a single polymer molecule meets this limitation, i.e. claim 30 embraces the subject matter of claims 1-29.

Claims 1-17, 20-23, 27, 28, 30-35, 40, 43-46, 50, 51, 53 and 54 are rejected under 35 U.S.C. 102(e) as being anticipated by Boles et al. US 5,932,711.

First, Claim 1 of Boles recites a "first subunit", i.e. the "first polymerizable ethylene-containing monomer unit", which is itself a polymer by virtue of both the nucleic acid and the poly (ethylene glycol) moieties. It comprises a nucleic acid derivatized to an α-acrylol, ω-N-hydroxysuccinimidyl ester of poly (ethylene glycol)-propionic acid. The "first subunit" of instant claim 1 could be the ethylene glycol subunit to which the nucleic acid is attached, or the nucleoside of the nucleic acid to which the ester is attached. In either case, the hydroxysuccinimidyl is a linker. Boles discloses that subunits such as described in claim 1, can be made by the process implied by instant claims 1 *inter alia*, e.g. a nucleotide derivatized with the α-acrylol, ω-N-hydroxysuccinimidyl ester of poly (ethylene glycol)-propionic acid, or any other ethylene containing moiety, can be added as a synthon during phosphoramidite synthesis of the nucleic acid (see col. 9, line 59 through col. 10, line 42).

Boles (col. 5, lines 20-30) discloses that the nucleic acid may be either single-strand or double-strand. Where the nucleic acid is double-strand, one strand meets the limitation of compacting moiety relative to the other since it causes a random coiled single strand into a helical conformation. Boles (col. 7-8) discloses that the nucleic acid-containing polymerizable ethylene-containing monomer units may comprise a linker group which is placed between the nucleic acid and the polymerizable ethylene moiety. The linkers can be cleavable chemically (including reduction of disulfide bonds), enzymatically, thermally, or by exposure to light. Boles

discloses that polymerizable ethylene moiety can be acrylate, acrylamide, methacrylate, methyl-methacrylate, hydroxyethylmethacrylate, *inter alia* Col. 10, lines 51-67). Boles also discloses polymeric beads comprising copolymers of polymerizable ethylene-containing monomer units that are unmodified and modified with nucleic acid (col. 8, line 51 to col. 9, line 23).

In so much as all chemical bonds can be cleaved by at least one of the processes recited in claim 5, for example, the limitations regarding "cleavable moiety" are met by any bond in the polymer, including bonds between subunits or between subunit and nucleic acid. Also, the nucleotide proximal to the polymer may be considered to be part of the "linker group" and the phosphodiester bond separating this nucleotide from the rest of the oligonucleotide is a cleavable bond of the linker group, and cleavable by a process in a biological system. With respect to "particle", e.g. claim 30, a particle is simply a "very small piece", consider "sub-atomic particle". Thus, a single polymer molecule, such as a nucleic acid-containing polymerizable ethylene-containing monomer unit, or polymeric beads meets this limitation, i.e. claim 30 embraces the subject matter of claims 1-29.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or

applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

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